Citation:

Banel DK, Hu FB. Effects of walnut consumption on blood lipids and other cardiovascular risk factors: a meta-analysis and systematic review. *Am J Clin Nutr*. 2009;90(1):56-63.

PubMed ID: 19458020

Study Design:

Systematic Review/Meta-analysis

Class:

M - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

- The aim of this systematic review was to perform a comprehensive assessment of the literature and carry out a meta-analysis by examining the change in lipid concentrations induced by a walnut-enhanced diet.
- Additionally, concerns were addressed regarding the issue of a walnut-enriched diet leading to weight gain.
- Finally, a qualitative review was performed of other CVD risk factors that have been investigated in relation to walnut consumption.

Inclusion Criteria:

- Controlled trial that evaluated a walnut-enriched diet compared with a control diet.
- Reported baseline and follow-up values, the mean change from baseline, or the mean differences between intervention groups for at least one lipid variable.
- Studies needed to have specifically tested walnut-based interventions and to have clearly stated the amount and frequency of walnuts included or instructed in the diet.

Exclusion Criteria:

- Trials that compared only the effects of nuts other than walnuts.
- Studies evaluating only postprandial effects because this outcome was not of primary interest.
- Excluded publications were retained for consideration in the review of nonlipid CVD risk factors.

Description of Study Protocol:

Recruitment

- Relevant English-language articles were identified by searching the Medline database and Cochrane Reviews through May 2008.

Design: Systematic review/random-effects meta-analysis

Blinding used Not applicable

Intervention

- Categorized by walnut consumption: specific amount of walnuts, control intervention

Statistical Analysis

- For the meta-analysis, the mean change from baseline to follow-up for each intervention and control group was calculated, if not reported.
- This was conducted by using a paired Student's *t* test to obtain the group mean and pooled SD. For studies providing only the mean difference between the walnut and the control groups, the control group's mean change was set as 0 and the walnut group's mean change was set as the reported mean difference. These studies were excluded from calculation of the percentage change (described below) because the control groups were artificially set at 0 and the actual mean change for each group was unknown.
- Standard errors and confidence intervals were converted to SD for the analyses.
- All serum lipid values were converted to milligrams per deciliter, if necessary.
- If more than one time point for follow-up was reported, we included the value closest to the time point used in the other studies for our primary analysis.
- For studies with more than one comparison group, we included the control diet most like the walnut diet after the exclusion of walnuts or other nuts.
- Additionally, studies without SD, SE, CIs, or a P value accompanying the mean values were excluded from analysis but retained for discussion.
- The METAN command in STATA version 9.0 was used to calculate a weighted mean difference (WMD) by conducting a random-effects meta-analysis.
- Cochrane's *Q* test was used to evaluate the significance of heterogeneity.
- In addition, the I^2 was produced and 95% CI with the command HETEROGI to evaluate the proportion of any heterogeneity due to between-study variation, with a $P<0.1$ level of significance.
- Sensitivity analyses were performed to evaluate the effect of outliers or "effect modifiers".
- It was hypothesized that the amount of walnuts per day (% energy from fat), follow-up time, baseline comorbidity status, or type of control diet could potentially modify the observed effects between studies.
- A sensitivity analysis was also conducted to assess the effect of study quality on outcomes.
- For this, a subgroup was made up of crossover randomized trials with a Jadad score of 3 or higher.
- Studies reporting poor compliance (as defined by the author or authors) were excluded from this subgroup.
- The percentage change from the WMD was derived for the intervention and control groups, divided by the weighted mean baseline levels, and multiplied by 100.
- Publication bias was assessed through Egger's and Begg's tests for each outcome at the $P<0.05$ level of significance. The authors also visually inspected Begg's funnel plot for publication bias, looking for any skewing to either side of the effect estimate.

Data Collection Summary:

Timing of Measurements

- Publication dates ranged from 1993 through 2008.

Dependent Variables

- BMI and weight change
- Blood lipid values

Independent Variables

- Walnut consumption

Control Variables

- None specifically listed; however, confounding factors/mediators were accounted for by inclusion/exclusion criteria.

Description of Actual Data Sample:

Initial N: 889 citations

Attrition (final N):

- 27 articles were retrieved for complete review (Figure 1 shows attrition diagram).
- 13 studies included in the meta-analysis of serum lipid concentrations, representing a total of 365 participants.

Age: varied with the individual studies; ranged from 24 to 66 years of age

Ethnicity: not given

Other relevant demographics:

- 12 studies were randomized trials, 10 of which had a crossover design.
- The baseline characteristics and comorbidity status of the participants varied.

Anthropometrics

- Patient characteristics of the individual studies are given in Table 1 of the article.
- Patients included healthy, overweight/obese, metabolic syndrome, Type 2 diabetes, hypercholesterolemia.
- Four studies recruited only those with healthy cholesterol concentrations, whereas 6 studies included participants with modest hypercholesterolemia.
- The remaining studies evaluated the effect of the walnut intervention among patients with diabetes, older obese subjects, and participants with metabolic syndrome.

Location: International studies

Summary of Results:

Key Findings:

- The meta-analyzed WMD shows a significantly greater reduction in TC while consuming a

walnut-enriched diet than a control diet (WMD=-10.29 mg/dL, P<0.001). This difference represents a 4.9% greater decrease in TC concentration while consuming walnuts.
- Individual study trends for LDL cholesterol were similar to those of TC. The overall result indicated a 6.7% significantly greater decrease in LDL-cholesterol concentration with the walnut intervention diets compared with the control diets (WMD=-9.23 mg/dL, P< 0.001).
- Overall, there was not a significant difference in serum HDL between walnut-enriched diets and control diets (WMD= -0.20 mg/dL, P=0.80).
- Triglyceride concentrations during walnut and control diets decreased by 12.5% and 9.1% from baseline, respectively. Although differences in triglyceride change did not reach statistical significance, a trend was observed in favor of walnut diets (WMD=-3.86 mg/dL, P=0.35).
- The treatment effect was not significantly different between studies.
- The 6 studies among participants with hypercholesterolemia produced results similar to the overall meta-analyses, which slightly favored walnut diets (TC: WMD=-12.0, P<0.001; LDL cholesterol: WMD=-10.1, P<0.001; HDL cholesterol: WMD= 1.1, P=0.4; triglycerides: WMD = -6.0, P=0.3).
- The dose-response effect of walnut amount (% total energy) and weeks of intervention had no effect.
- There were no signs of publication bias.
- None of the studies reported significant weight change while on a walnut-based intervention.
- Of the other CVD risk factors, few reached statistical significance and were consistent across studies.
- 3 studies found significantly greater decreased in apo B for the walnut group than for the control group.
- Markers of oxidative stress maintained baseline concentrations across all interventions, indicating no increased oxidative stress over the duration of the trials. Importantly, resistance to oxidation was maintained despite reported increases in lipid particle enrichment with polyunsaturated fatty acids.
- Results for C-reactive protein were inconsistent across the studies.
- Overall, evidence of decreasing VCAM-1 and increasing endothelium-dependent vasodilation suggests that walnut-rich diets may have benefits for vascular endothelial function, a mediator of CVD risk.

Author Conclusion:

- Overall, high-walnut-enriched diets significantly decreased total and LDL cholesterol for the duration of the short-term trials.
- Larger and longer-term trials are needed to address the effects of walnut consumption on cardiovascular risk and body weight.

Reviewer Comments:

Authors note the following limitations:

- *Studies had relatively small sample sizes and short durations of follow-up; the longest follow-up time was 6 months so presumed health benefits cannot be extrapolated beyond the duration of these studies*
- *The amount of walnuts consumed in these trials was relatively large, representing 5 - 25% of*

total calories (30 - 108 g/day), which might be difficult to maintain in a non-research setting

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Research Design and Implementation Criteria Checklist: Review Articles

Relevance Questions		
1.	Will the answer if true, have a direct bearing on the health of patients?	Yes
2.	Is the outcome or topic something that patients/clients/population groups would care about?	Yes
3.	Is the problem addressed in the review one that is relevant to nutrition or dietetics practice?	Yes
4.	Will the information, if true, require a change in practice?	Yes

Validity Questions		
1.	Was the question for the review clearly focused and appropriate?	Yes
2.	Was the search strategy used to locate relevant studies comprehensive? Were the databases searched and the search termsused described?	Yes
3.	Were explicit methods used to select studies to include in the review? Were inclusion/exclusion criteria specified and appropriate? Were selection methods unbiased?	Yes
4.	Was there an appraisal of the quality and validity of studies included in the review? Were appraisal methods specified, appropriate, and reproducible?	Yes
5.	Were specific treatments/interventions/exposures described? Were treatments similar enough to be combined?	Yes
6.	Was the outcome of interest clearly indicated? Were other potential harms and benefits considered?	Yes
7.	Were processes for data abstraction, synthesis, and analysis described? Were they applied consistently across studies and groups? Was there appropriate use of qualitative and/or quantitative synthesis? Was variation in findings among studies analyzed? Were heterogeneity issued considered? If data from studies were aggregated for meta-analysis, was the procedure described?	Yes
8.	Are the results clearly presented in narrative and/or quantitative terms? If summary statistics are used, are levels of significance and/or confidence intervals included?	Yes
9.	Are conclusions supported by results with biases and limitations taken into consideration? Are limitations of the review identified and discussed?	Yes
10.	Was bias due to the review's funding or sponsorship unlikely?	???